## REMARKS

In the Office Action mailed from the United States Patent and Trademark Office on 11/30/07, the Examiner rejected claims 6-49.

Interview

The Applicants representative and the Examiner conducted a telephonic interview on 2/25/08. The topics discussed are included in the claim amendments and the remarks section of this document.

Double Patenting

In the Office Action, the Examiner noted that claims 6-11, 15, and 19 are rejected under the judicially created doctrine of obviousness-type double patenting for reciting subject matter that is unpatentable over claims 6-11, 15, and 19 of copending application 10/269,422 in view of U.S. Pat. No. 5,522,798 to Johnson. Applicants request that the obviousness-type double patenting rejection be held in abeyance until all other issues have been resolved in the above-referenced application.

Rejections under 35 U.S.C. § 102

In the Office Action, the Examiner rejected claims 6, 8-10, 12-30, 35, and 41-50 under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. No. 5,088,981 to Howson. Applicants respectfully traverse. The standard for a Section 102 rejection is set forth in M.P.E.P 706.02, which provides:

> "… for anticipation under 35 U.S.C. 102, the reference must teach every aspect of the claimed invention either explicitly or impliedly. Any feature not directly taught must be inherently present."

Applicants have amended independent claims 6, 14, and 35 to clarify the distinctions with the cited reference. Applicants recognize the challenges associated with language in this field in relation to the claimed invention and have attempted to further clarify the term **probability of effectiveness,** which utilizes both modeled Pk (pharmacokinetic) AND Pd (pharmacodynamic) data. This is distinguished from conventional **effect** site concentration, **effect** compartment concentration, and dosage, which are based entirely on modeled Pk data only.

> "Howson et al. **does not explicitly teach** a drug display monitor configured to depict, in real time, a present probability of effectiveness … However, the examiner views a computer monitor being capable and already configured to display any type of data stream…". Office Action, Pages 5-7.

Independent claims 6, 15, and 35 have been amended to clarify that the claimed systems include an **algorithm** to mathematically determine the present probability of effectiveness. The inclusion of an algorithm clarifies that the probability of effectiveness is determined by the claimed systems rather than being received as a data stream. One embodiment of this algorithm is discussed in the specification with reference to a drug modeler/normalizer 2518 and is illustrated in the system schematic diagram Figure 25. Specification, page 43, line 20 – page 44, line 3. Howson fails to explicitly or implicitly teach a system that is configured to **determine** AND **display** a probability of effectiveness including a "…correlation of a predicted drug effect site concentration based on modeled pharmacokinetic data and a probability of achieving a bodily effect on the patient based on modeled pharmacodynamic data…".

In addition, claims 6, 15, and 35 have been amended to clarify the manner in which the probability of effectiveness is **displayed**. Figures 23 and 24 of specification illustrate one embodiment of displaying probability of effectiveness, including displaying predicted/modeled concentration (Pk) as a percent of a concentration value corresponding to a known (Pd)

probability of causing a particular bodily effect. Figure 24 represents one implementation embodiment of the invention and is therefore annotated in red below for technical and terminology clarification purposes.

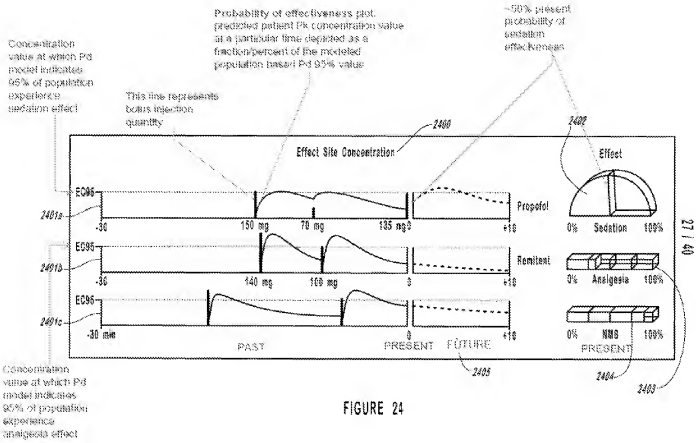


FIGURE 24

Amended Claim 6 includes,

> "…wherein the drug display monitor is configured to depict, in real time, the present and future probabilities of effectiveness including predicted pharmacokinetic effect site concentrations depicted as a percent of a concentration value corresponding to a known pharmacodynamic probability of causing a particular bodily effect".

Amended Claim 14 includes,

> "…a display monitor in communication with the graphics adapter and configured to depict, graphically and substantially in real-time, the modeled probability of effectiveness including predicted pharmacokinetic effect site concentrations depicted as a percent of a concentration value corresponding to a probability of causing a particular bodily effect including at least one of:
>
> causing the subject to lose consciousness;

eliminating or blocking laryngoscopy pain, incision pain, or intraoperative pain; and

causing a measurable level of muscle relaxation.".

Amended Claim 35 includes,

> "…an output element configured to display, substantially in real-time, the modeled concentration of the at least one drug normalized in reference to at least one concentration at which the at least one drug will have a desired pharmacodynamic effect on a known percentage of a population."

Howson fails to **determine** OR **displa**y a probability of effectiveness consistent with the claimed systems. Rather, Howson teaches a system for programming a desired flow rate for a portable infusion pump so as to achieve a desired predicted concentration (Pk). Abstract. While Howson may use pharmacokinetic (Pk) models 26 with a display 28 to predict plasma and effect-site concentrations in the past, present and future, it does not teach the inclusion of an algorithm that **correlates** pharmacodynamic (Pd) models with effect-site concentration (Pk) to accurately **display** a probability of effectiveness at causing a bodily effect such as sedation, analgesia, and NMB. Rather, a user of Howson is forced to **interpret/assume/calculate** that a particular concentration has a desired pharmacodynamic bodily effect. Unfortunately, numerous well known clinical cases have occurred in which a patient experienced pain or regained consciousness despite the Pk-based **assumption** that the particular effect site concentration was sufficient to maintain the desired pharmacodynamic bodily effect (ie. anesthesia, analgesia, NMB). The study of pharmacodynamics is based on accurately predicting how the body responds to a particular drug. While particular concentrations may be commonly **assumed** to produce a particular bodily effect, this assumption is known to sometimes be false.

For at least these reasons, Applicants request that the rejection of independent and corresponding dependent claims 6, 8-10, 12-30, 35, and 41-50 be withdrawn.

Rejections under 35 U.S.C. § 103

In the Office Action, the Examiner rejected claims 7 and 11 under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,088,981 to Howson as applied to claims 6, 8-10, 12-13, 15, 20-21, and 41-43 in view of U.S. Pat. No. 5,925,014 to Teeple. Applicants respectfully traverse.

Claims 7 and 11 are dependent from independent claim 6 and therefore are allowable for at least the reasons stated above.

Teeple teaches an infusion pump type system that is **limited to** pharamacokinetic data to determine an appropriate flow rate so as to achieve a predicted Pk-based effect site concentration. Figure 4 of Teeple illustrates a chart of **infusion rates** designed to achieve particular Pk effect site concentrations for particular drugs. The prediction of a drug concentration, effect site concentration, or effect compartment concentration requires that a user **interpret/assume/calculate** that a particular concentration has a desired pharmacodynamic bodily effect. Teeple fails to teach the determination or display of probability of effectivness. Therefore, Teeple and Howson independently and in combination fail to teach the determination and display of probability of effectiveness as claimed in the present application.

In the Office Action, the Examiner rejected claims 31-34 and 36-40 under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 5,088,981 to Howson as applied to claims 6, 8-10, 12-13, 15, 20-21, and 41-43 in view of U.S. Pat. No. 5,522,798 to Johnson and further in view of U.S. Pat. No. 5,925,014 to Teeple. Applicants respectfully traverse.

Claims 31-34 and 36-40 are dependent from independent claim 15 and 35 and therefore are allowable for at least the reasons stated above.

Johnson teaches an infusion pump system that considers pharmacokinetic data in creating a flow rate designed to achieve a particular concentration (Pk). While Johnson may use pharmacokinetic (Pk) models to predict a concentration (Figure 5 elements, 126, 128, 132), it does not include an algorithm that **correlates** pharmacodynamic (PD) models with the predicted concentrations to **accurately display** predict a probability of pharmacodynamic bodily effect such as sedation, analgesia, and NMB. Rather, a user of Johnson is forced to **interpret/assume/calculate** that a particular Pk-based concentration has a desired pharmacodynamic bodily effect. Therefore, Johnson, Teeple and Howson independently and in combination fail to teach the determination and display of probability of effectiveness as claimed in the present application.

## CONCLUSION

Applicants submit that the amendments made herein do not add new matter and that the claims are now in condition for allowance. Accordingly, Applicants request favorable reconsideration. If the Examiner has any questions or concerns regarding this communication, the Examiner is invited to call the undersigned directly at 801-533-4095 or email at trent@bakeriplaw.com .

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